UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF OHIO
EASTERN DIVISION

IN RE: NATIONAL PRESCRIPTION OPIATE LITIGATION	)	**MDL 2804**
	)	
	)	**Case No. 1:17-md-2804**
THIS DOCUMENT RELATES TO:	)	
	)	**Judge Dan Aaron Polster**
Track One Cases	)	
	)	**OPINION AND ORDER GRANTING IN PART DEFENDANTS' MOTION TO EXCLUDE MARKETING CAUSATION OPINIONS OF SCHUMACHER, LEMBKE, AND KEYES**

Before the Court is Defendants' Motion to Exclude the Marketing Causation Opinions of Mark Schumacher, Anna Lembke, and Katherine Keyes (**Doc. #: 1868**). For the reasons and to the extent stated below, the Motion is **GRANTED IN PART**.

* * * * *

Schumacher and Lembke are medical doctors, with expertise in pain medicine and addiction, who offer opinions about, *inter alia*, misleading and inaccurate information contained in Defendants' marketing and promotional materials. As part of these opinions, Schumacher and Lembke conclude this alleged misinformation influenced the prescribing practices of physicians, thereby resulting in increased prescriptions of opioids. Keyes, on the other hand, is an epidemiologist who specializes in opioid-related harm. She offers opinions about harms in the population related to increased opioid supply and misuse, including that increases in the supply of prescription opioids resulted in an exponential increase in prescription opioid overdose. As part

of this opinion, Keyes states that inaccurate marketing information contributed to the increase in the supply of prescription opioids.

Defendants assert all three witnesses lack the necessary qualifications to testify as an expert on pharmaceutical marketing and its alleged causation of opioid overdose and related harms. In addition, Defendants assert these opinions are unreliable and would mislead, confuse, and unfairly prejudice the jury.

The Court agrees that, although Schumacher and Lembke are distinguished experts in the medical fields of pain and addiction, they lack the specialized training or experience necessary to testify as experts about pharmaceutical marketing causation. Also, as to Keyes, the Court finds that, although she is highly qualified as an expert in epidemiology, Plaintiffs have not shown this expertise extends to her opinions on marketing causation in this case. Accordingly, as to these three witnesses, the Court will exclude the limited portions of their opinions that purport to find *causation* with respect to the effect that Defendants' marketing efforts had on increased sales and/or increased prescriptions of opioids. As discussed below, this ruling applies narrowly – that is, it excludes only to these witnesses' opinions regarding marketing causation and does not impact their remaining opinions in any way. The Court's reasoning is set forth below.[1]

I. Schumacher.

A. Credentials and Experience.

Schumacher received an M.D. and Ph.D. degrees in Physiology and Pharmacology from the University of California, San Diego. *See* Defs. Mtn. to Excl. Mktg. Causation Ops., Ex. 6 at 1

[1] The Court hereby incorporates the legal standards set forth in the Court's Opinion and Order regarding Defendants' motion to exclude the opinion and testimony of Prof. Meredith Rosenthal, see Doc. #: 2495.

("Schumacher CV") (Doc. #: 1868-9). He is currently a Professor and Chief of the Division of Pain Medicine in the Department of Anesthesia and Preoperative Care at the University of California, San Francisco. Over the past 24 years, Schumacher has devoted his academic career to advance pain medicine, through clinical care and research. *See id.* at 2; Defs. Mtn. to Excl. Mktg. Causation Ops., Ex. 5 at 7 ("Schumacher Rpt.") (Doc. #: 1868-8).

Schumacher served as one of 18 members on the National Academies of Sciences, Engineering, and Medicine ("NASEM") Committee on Pain Management and Regulatory Strategies to Address Prescription Opioid Abuse, which published a Consensus Report in July of 2017. *See* Schumacher Rpt. at 7, 27 (Doc. #: 1868-8); Pls. Opp., Ex. 1 ("Consensus Report") (Doc. #: 2166-1). The Committee described its task as: "to review and assess approaches and actions that the Federal Drug Administration ("FDA") and others have taken, and could take, to resolve the [opioid epidemic] and prevent such problems from arising in the future." Consensus Report at 40 (Doc. #: 2166-1).

B. Opinions.

Schumacher offers the following opinions:

(1) the medical standard of care for treating chronic and acute pain changed as a result of Defendants' widespread promotion and marketing of opioids that trivialized the risk of addiction and exaggerated the benefits of long-term opioid use;

(2) through direct physician marketing, medical education, and industry-sponsored and industry-funded Key Opinion Leaders ("KOLs"), Defendants influenced physicians to prescribe long-term opioids based on misinformation about the risks and benefits of chronic opioid use;

(3) for the vast majority of chronic pain patients, the risks of prescription opioids significantly outweigh any benefits; and

(4) even in situations where opioids are effective in treating pain, the risks are so significant that non-opioid alternatives should be used whenever possible.

See Schumacher Rpt. at 6-7 (Doc. #: 1868-8).

Part of Schumacher's second opinion involves "marketing causation." As to this opinion, Schumacher reviewed discovery materials in this case and identified dozens of marketing efforts by Purdue and other Defendants, finding they contained false and/or misleading messages about prescription opioids that minimized the risks of addiction and misrepresented and/or exaggerated the benefits, including statements that more potent and long-acting formulations of opioids (such as OxyContin) were safe and effective in the treatment of chronic, non-cancer pain. *See id.* at 30-41. Schumacher opines that, to increase the sales of prescription opioids, Purdue and other Defendants delivered these messages through: (i) direct marketing to physicians and consumers; (ii) funding of research, pain-related medical societies, and continuing medical education; (iii) lobbying medical boards and agencies responsible for pain-related treatment guidelines; and (iv) lobbying state and local governments to remove barriers to broader use of opioids for the treatment of pain. *See id.* at 28-29. Schumacher states these efforts influenced physicians to replace a cautious and conservative approach to the use of opioids with much more liberal prescribing practices, thereby causing a significant increase in the number of opioid prescriptions. *See id.* at 21, 28-30.

Schumacher notes "there are a number of reasons" why the opioid epidemic was able to take root in the United States, including: (i) a lack of medical education on the treatment of pain and (ii) market forces that reduced the availability of multidisciplinary pain treatment. *See id.* at

26-27. However, Schumacher also states: "there is no real question that the epidemic has been driven by an unwarranted increase in prescription opioids orchestrated by the pharmaceutical industry." *Id.* at 27. More specifically, he opines:

> the driving force of this national catastrophe has been the introduction and marketing of long-acting formulations of high potency opioids such as OxyContin in 1996. Physicians were misled through Defendants' marketing and sales detailing intended to persuade doctors to accept that more potent and long-acting formulations of opioids (such as OxyContin) were safe and effective . . . and even at high doses.

Id. at 28. It is this "marketing causation" opinion that Defendants seek to exclude.

C. Analysis.

Defendants assert Schumacher is not qualified to testify as an expert on marketing causation because he has no specialized expertise or experience in this field. *See* Defs. Mem. at 4 (Doc. #: 1862-2). Plaintiffs respond that Schumacher's "most relevant and significant credential" regarding marketing causation is his participation on the NASEM Committee on Pain Management, which they contend "reached a consensus that Defendants' marketing contributed causally to the opioid epidemic." Pls. Opp. at 2 (Doc. #2166). But the Committee specifically stated it was not directed to investigate the cause of the opioid epidemic and "did not aim to assign responsibility" in this regard. Consensus Report at 40 (Doc. #: 2166-1). Plaintiffs point to statements by the Committee that "certain hypotheses" about causation are "inescapable" and that certain data makes a "prima facie case" that Manufacturers' marketing and increased prescribing by physicians were "key contributors" to the increase in opioid use.[2] Pls. Opp. at 2-3 (Doc. #2166)

[2] The Committee also stated:

> It is also clear, however, that overprescribing was not the sole cause of the problem. While increased opioid prescribing for chronic pain has been a vector of the opioid epidemic, researchers agree that such structural factors as lack of economic

(quoting Consensus Report at 40-41 (Doc. #: 2166-1). On their face, these statements do not indicate that the Committee made causation findings. *See, e.g.* Merriam-Webster Online (https://www.merriam-webster.com/dictionary/hypothesis) ("hypothesis" means "a tentative assumption made in order to draw out and test its logical or empirical consequences"); (https://www.merriam-webster.com/dictionary/prima%20facie) ("prima facie" means "true, valid, or sufficient at first impression"). Moreover, even if the Committee made causation findings (which it apparently did not), Plaintiffs have not shown the extent of Schumacher's involvement therein.

To qualify as an expert under Rule 702, a witness must establish his expertise through "knowledge, skill, experience, training, or education," Fed. R. Evid. 702, and the expert's training and qualifications must "relate to the subject matter of his proposed testimony." *Rose v. Truck Ctrs., Inc.,* 611 F. Supp.2d 745, 749 (N.D. Ohio 2009) (citation omitted). Here, the record demonstrates that Schumacher is highly distinguished as an expert in the scientific disciplines of physiology, pharmacology, and pain medicine. He is, therefore, "fully qualified" to opine on matters involving medical facts and science that fall within these subject areas. *In re Diet Drugs Prods. Liab. Litig.,* 2000 WL 876900, at *11 (E.D. Pa. June 20, 2000). Plaintiffs have not shown, however, that Schumacher has specialized training, knowledge, or experience in the field of pharmaceutical marketing. *See* Defs. Mtn. to Excl. Mktg. Causation Ops., Ex. 9 at 30:9 to 31:5 ("Schumacher Depo.") (Doc. #: 1868-12) ("I have not stated I've ever been an expert in

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> opportunity, poor working conditions, and eroded social capital in depressed communities, accompanied by hopelessness and despair, are root causes of the misuse of opioids and other substances[.]

Id. at 40-41. Thus, while the Committee noted that heavy promotion and increased prescribing were "key contributors," it also recognized that these factors were not the "sole cause" of the opioid epidemic and other factors contributed as well. *See id.*

marketing."); *see also Diet Drugs,* 2000 WL 876900, at *9-11 (concluding medical doctors did not have specialized knowledge or experience in the way the pharmaceutical marketplace reacts, behaves, or thinks).

On this record, the Court finds Schumacher may not testify regarding the effect of Defendants' marketing efforts on doctors' prescribing practices.[3] *See, e.g., Pfizer Inc. v. Teva Pharm. USA, Inc.*, 461 F. Supp.2d 271, 277 (D.N.J. 2006) (medical doctor may not opine regarding the effect that marketing materials had on doctors' prescribing practices); *Bartlett v. Mut. Pharm. Co.*, 742 F. Supp.2d 182, 195 (D.N.H. 2010) (most courts have prohibited doctors from testifying as experts "about what all doctors generally think in making prescription decisions") (quoting *Diet Drugs,* 2000 WL 876900, at *11-12). This ruling applies narrowly, only to the small portion of Schumacher's second opinion (listed above) that purports to find that Defendants' marketing efforts resulted in increased sales and/or increased prescriptions of opioids. The Court's ruling does not in any way impact Schumacher's remaining opinions, including the remainder of his second opinion regarding the inaccuracy of statements and representations made in marketing materials and other promotional and/or educational efforts.[4] *See, e.g., In re Gadolinium-Based Contrast Agents Prod. Liab. Litig.*, MDL No. 1909, 2010 WL 1796334, at *19 (N.D. Ohio May 4, 2010) (nephrologist may offer opinions on whether labeling and marketing information contained inaccuracies or omissions that could deprive or mislead physicians, like himself, who treated

[3] In light of this ruling, the Court does not address Defendants' arguments that Schumacher's opinions on marketing causation are unreliable and unfairly prejudicial.

[4] The Court notes that Defendants' motion does not address Schumacher's first opinion, *i.e.* that the medical standard of care for treating chronic and acute pain changed as a result of Defendants' widespread promotion and marketing of opioids, or his third and fourth opinions. Accordingly, the Court's ruling does not in any way affect Schumacher's ability to testify regarding these opinions.

renally impaired patients); *Pfizer,* 461 F. Supp.2d at 277 (doctor may render an opinion on the accuracy of defendant's marketing materials).

II. Lembke.

A. Credentials and Experience.

Lembke received an M.D. degree from the Stanford University School of Medicine in 1995, and also completed there a partial residency in Pathology (1997), a full residency in Psychology (2000), and a Fellowship in Mood Disorders (2002). *See* Defs. Mtn. to Excl. Mktg. Causation Ops., Ex. 3 at 1 ("Lembke Rpt.") (Doc. #: 1868-6). Since 2003, Lembke has served on the faculty at Stanford, where she has taught medical students, residents, and fellows on a variety of topics related to psychiatry, addiction, and pain. *See id.* As a full-time faculty member, Lembke regularly treats patients who are addicted to opioids and other substances. *See id.* For the last 15 years, her clinical practice "has included a significant proportion of patients taking prescription opioids for pain relief, for whom such drugs have resulted in misuse, dependence, and addiction." *Id.* Lembke also sees patients at the Stanford Pain Clinic, where she provides expert consultation in pain and addiction. *See id.*

B. Opinions.

Lembke offers the following opinions:

(1) an explanation of what addiction is and its causes, including that one of the biggest risk factors for addiction is simple access to addictive drugs, *see* Lembke Rpt. at 7-9 (Doc. #: 1868-6);

(2) opioid prescribing in the United States began to increase in the 1980s and became prolific in the 1990s and early 2000s, creating more access to opioids and representing a radical paradigm shift in the treatment of pain, *see id.* at 9-14;

(3) the Pharmaceutical Industry increased sales of prescription opioids by convincing prescribers that liberal opioid prescribing is based on science through: (a) directly targeting doctors; (b) promoting key opinion leaders; (c) infiltrating continuing medical education ("CME") courses; (d) supporting professional medical societies; and (e) co-opting medical watchdog organizations like The Joint Commission, *see id.* at 14-21;

(4) in the absence of reliable scientific evidence, the Pharmaceutical Industry encouraged and promoted several misconceptions through: (a) misleading marketing and promotional claims concerning opioid use, including overstatements about its benefits for long-term use for chronic pain, *see id.* at 21-37; (b) understatements about the risks of addiction, *see id.* at 37-63; inaccurate claims as to the levels at which doses can be safely increased, *see id.* at 63-66; (c) mischaracterizing addictive behavior as "pseudoaddiction" and tolerance as "breakthrough pain," *see id.* at 66-68; (d) characterizing opioid dependence as a benign state that is easily reversible, *see id.* at 68-73; and (e) inaccurate claims as to the validity of patient screening as a predictor of who will become addicted, *see id.* at 73-63;

(5) the Pharmaceutical Opioid Industry's actions "significantly influenced doctors" and these misconceptions were "the single most significant factor" giving rise to

the massive increase in opioid sales and resulting epidemic of dependence and addiction, *see id.* at 75-81;

(6) the increase in sales resulted in a prescription opioid epidemic in the United States, s*ee id.* at 81-84;

(7) a clear link exists between prescription opioid exposure and the subsequent use of heroin and other illicit opioids, *see id.* at 84-86;

(8) the increase in sales of prescription opioids harmed communities in various ways, *see id.* at 86-89; and

(9) ending the epidemic will require a significant investment of resources and an effective, multifaceted strategy, *see id.* at 89-97.

Part of Lembke's third and fifth opinions involve marketing causation. Regarding these opinions, after recounting dozens of examples of what she contends were false and misleading messages and actions by Manufacturers and the Opioid Pharmaceutical Industry, Lembke opines that these actions "significantly influenced doctors" and "directly contributed" to the opioid epidemic by "successfully encourag[ing] doctors into believing the risks of addiction were low, which directly contributed to increased subscribing." *Id.* at 58, 75. Lemke concludes the ongoing opioid epidemic "is the result of aggressive marketing and promotion of such drugs." *Id.* at 97.

C. Analysis.

Defendants assert Lembke is not qualified to testify as an expert on marketing causation because she has no specialized expertise or experience in this field. *See* Defs. Mem. at 4-5 (Doc. #: 1862-2). Plaintiffs respond that, of great "significance in this context," is the book that Lembke published in 2016, entitled *Drug Dealer, MD: How Doctors Were Duped, Patients Got Hooked, and Why It's so Hard to Stop.* Pls. Opp. at 3-4 (Doc. #2166). Plaintiffs assert that, in this book,

Lembke described the "misconceptions" that Defendants promoted and, in her Report, Lembke relied on the NASEM Committee's findings (discussed above) in support of her opinion that the increase in opioid prescriptions "is causative" of the rising rates of opioid addition and related deaths. *Id.* (quoting Lembke Report at 4 (Doc. #: 1868-6)). In their response, however, Plaintiffs point to no specialized training or experience by Lembke in the field of pharmaceutical marketing and/or its effect on prescribing practices, or the field of economics.[5]

Plaintiff's response falls short of establishing that Lembke is qualified through "knowledge, skill, experience, training, or education" to testify as an expert on marketing causation. Fed. R. Evid. 702; *see also Rose,* 611 F. Supp.2d at 749 (expert's training and qualifications must relate to the subject matter of her proposed testimony). Similar to Schumacher, the record demonstrates Lembke is highly distinguished as a medical expert in the scientific disciplines of psychiatry, addiction, and pain. She is therefore "fully qualified" to opine on matters involving medical facts and science that fall within these areas. *Diet Drugs*, 2000 WL 876900, at *11. However, Plaintiffs have not shown Lembke has specialized training, knowledge, or experience in the field of pharmaceutical marketing. *See* Defs. Mtn. to Excl. Mktg. Causation Ops., Ex. 2 ("Lembke CV") (Doc. #: 1868-5); *see also Diet Drugs,* 2000 WL 876900, at *9-11.

[5] The Court rejects Plaintiffs' arguments that, because Lembke formed her opinions based at least in part on her review and assessment of scientific literature on this topic, she is qualified to opine on marketing. *See* Pls. Mem. at 6-10 (Doc. #: 2166); *In re Welding Fume Prod. Liab. Litig.*, No. 1:03-cv-17000, MDL 1535, 2005 WL 1868046, at *35 (N.D. Ohio Aug. 8, 2005) (a person does not become an expert in an area outside of her regular field merely by "reading up" for the specific purpose of testifying); *Hutson v. Covidien Holding, Inc.,* No. 2:13-cv-895, 2015 WL 4040447, at *4 (S.D. Ohio June 30, 2015) (an expert must make some findings and not merely regurgitate another expert's opinion); *cf. Smith v. Pfizer, Inc.*, 714 F. Supp.2d 845, 855-56 (M.D. Tenn. 2010) (allowing an *economist* to testify regarding the results of a prescription drug marketing campaign).

On this record, Plaintiffs have not shown that Lembke is qualified to testify as an expert on marketing causation. *See, e.g., Pfizer,* 461 F. Supp.2d at 277; *Bartlett,* 742 F. Supp.2d at 195; *see also In re Seroquel Prod. Liab. Litig.* 2009 WL 3806436, at *8 (M.D. Fla. July 20, 2009) (medical doctor may testify as an expert on the accuracy of information in marketing materials but may not opine on what a drug company intended or sought to achieve through the use of those materials). Accordingly, the Court finds Lembke may not testify regarding the effect that Defendants' marketing and promotional efforts had on doctors' prescribing practices.[6] Again, this ruling applies narrowly, only to the portions of Lembke's third and fifth opinions (listed above) that purport to find Defendants' marketing efforts resulted in or caused increased sales and/or increased prescriptions of opioids. The Court's ruling does not in any way affect Lembke's remaining opinions, including the remainder of her third and fifth opinions regarding the inaccuracy of statements and representations in Defendants' marketing materials and other promotional and/or educational efforts. *See, e.g., In re Gadolinium-Based Contrast Agents,* 2010 WL 1796334, at *19; *Pfizer,* 461 F. Supp.2d at 277 (doctor may render an opinion on the accuracy of defendant's marketing materials). In other words, for instance, this ruling does not prevent Lembke from expressing, under her third opinion, that the Defendants misrepresented the risks and benefits of opioids, and how they did so. Rather, this ruling applies only to Lembke's opinion regarding a causal connection with respect to pharmaceutical marketing, *i.e.* that Defendants' marketing efforts resulted in increased sales and/or increased supply of prescription opioids. Similarly, under her fifth opinion, Lembke may testify about the allegedly misleading nature of the materials that she says Manufacturers disseminated to prescribers and how doctors, in general,

[6] In light of this ruling, the Court does not address Defendants' arguments that Lembke's opinions on marketing causation are unreliable and unfairly prejudicial.

rely on such information in making prescribing decisions. *See, e.g., id.* at 75-81. She may also testify regarding the direct experiences she and her colleagues have had with Defendants' marketing of opioids. Lembke may not, however, testify as to the causal effect of these actions, *i.e.* she may not opine that these actions caused an increase in the sales and/or supply of prescription opioids.

III. Keyes.

A. Credentials and Experience.

Keyes received a Master's degree in Public Health in 2004 and a Ph.D. in Epidemiology in 2010, both from Columbia University. *See* Defs. Mtn. to Excl. Mktg. Causation Ops., Ex. 1 at 1 ("Keyes Rpt.") (Doc. #: 1868-4). She is currently an Associate Professor of Epidemiology at Columbia, where she specializes in the epidemiology of substance use and substance-use disorders, including opioid use and related harms. *Id.* at 1-2. She has published 225 peer-reviewed articles and book chapters, and two textbooks on epidemiological methods. *Id.* at 1-2.

Keyes' expertise on opioid-related harm includes "large scale survey data and vital statistics analyses, as well as the development of theories, hypotheses, and publishing findings concerning the role of macro-social factors in producing opioid epidemics." *Id.* at 2. More specifically, Keyes has "extensively used high-quality survey data collected at the national level in order to estimate incidence, prevalence, and trends in risk factors for opioid use disorders, and trends in opioid use." *Id.* In addition, she has "utilized data on fatal and non-fatal overdose to estimate determinants of variation in overdose across communities." *Id.* Keyes has published 19 peer-reviewed journal articles on opioid use and related harms, "detailing trends over time in prescription opioid misuse, birth cohort trends in nonmedical opioid use and overdose, and risk factors for non-medical prescription opioid use, and consequences of use across developmental

periods, including consequences related to overdose." *Id.* She has particularly focused on "elucidating drivers of population-level trends, including literature reviews, synthesis, and empirical analyses of urban-rural differences in nonmedical opioid use and overdose." *Id.*

With regard to assessing opioid-related harm, Keyes describes the role of epidemiology to quantify: (1) the extent to which opioid use, and harms associated with opioid use, are changing over time; (2) the determinants of those changes; and (3) the individual-level risk factors for non-medical opioid use and related harm. *Id.* at 8. In assessing the causes of the opioid crises, Keyes applied a "risk factor" framework, where a given risk factor is considered "be [a] cause[] of opioid use disorders, overdose, and related harm if some cases would not have occurred in the absence of prescription opioid use." *Id.* Keyes states: "[t]his framework does not preclude or ignore that addiction and related harms are multi-factorial in their etiology, but rather asks whether there are cases for which the outcome would not have occurred without the presence of prescription opioid use." *Id.*

In reaching her opinions, Keyes reviewed various literature and studies to "assess the impact of opioid sales and distribution in the United States on opioid use disorders and addiction, overdose, diversion, transition to heroin, as well as the evidence-based recommendations for abatement." *Id.* In so doing, Keyes relied on the methodology that she states is considered standard in the scientific process. *See id.* First, she searched for peer-reviewed literature related to the areas of her review. Keyes states that, while peer-review is considered to be "the gold-standard," peer-review alone is not sufficient to establish the quality and validity of a scientific study. *Id.* Thus, Keyes also performed her own review of the articles, based on her experience, "in order to discern whether they meet quality benchmarks." *Id.* at 8-9. In addition, Keyes included additional studies that she found relevant to each topic, as well as non-peer-reviewed

"gray" literature.[7] *Id.* at 9. Keyes' Report includes two general categories of evidence: (1) studies that examined associations; and (2) studies that examined trends over time. *See id.* at 9-10. Regarding studies that examined associations, Keyes considered the following levels of evidence: (1) randomized controlled trials, meta-analysis, and systematic reviews, which she designates as high levels of evidence; (2) studies that had prospective follow-up of participants, a well-described strategy for statistical control of confounders, and well-designed comparison groups, which she designates as the next level of evidence; and (3) well-designed studies of single populations without explicit comparison groups, which she designates as relevant evidence. *See id.* at 9-10. Regarding studies that examined trends over time, Keyes considered three data sources to be the highest levels of evidence: (1) death records that are collected and harmonized by the national vital statistics surveillance system; (2) data sources with national reputation for transparency in reliability and validity that assess hospitalization and other clinical records; and (3) survey data that is routinely collected in the general population of households in the United States over time. *See id.* at 10.

B. Opinions.

Keyes offers the following opinions:

[7] Keyes' Report does not define the term "gray" literature. The Twelfth International Conference on Grey Literature in Prague in 2010 defined it as a term that: "stands for manifold document types produced on all levels of government, academics, business and industry in print and electronic formats that are protected by intellectual property rights, of sufficient quality to be collected and preserved by libraries and institutional repositories, but not controlled by commercial publishers; *i.e.* where publishing is not the primary activity of the producing body." Duke University Medical Center Library & Archives, Systematic Reviews: the process: Grey Literature, https://guides.mclibrary.duke.edu/sysreview/greylit (last checked August 25, 2019).

(1) the distribution, sales, and marketing of opioids increased in the 1990s, *see id.* at 10-11.[8]

(2) the risk of opioid use disorder after the medical use of prescription opioids follows a "dose-response" pattern, *see id.* at 11-16;

(3) individuals with opioid use disorder diverted opioids for non-medical use, *see id.* at 16-18;

(4) the incidence and prevalence of non-medical use increased in concert with the increased supply of prescription opioids, *see id.* at 18-20;

(5) the increase in the prescription opioid supply, coupled with opioid use disorders and increases in non-medical use, resulted in an exponential increase in prescription opioid overdose, *see id.* at 20-25;

(6) increases in neonatal abstinence syndrome are one of the key indicators of opioid-related harm in the population, *see id.* at 25;

(7) prescription opioid use is causally related to heroin use, *see id.* at 25-27;

(8) the uptake of diverted opioids was not random, but part of a complex system that involved community level economic conditions, *see id.* at 27-28;

(9) all available evidence indicates that prescription opioid harms, due to medical use as well as diversion, increase with the supply of opioids, *see id.* at 28-29; and

[8] Regarding this first "opinion," Keyes states: "[t]here is voluminous evidence regarding the distribution, sales, and marketing of opioids beginning in the 1990s . . . [that] is the subject of other witnesses' reports." *Id.* at 10. For "context," Keyes summarizes some key points, including that: "[e]vidence shows that pharmaceutical marketing of prescription drugs increases prescribers' likelihood of prescribing the marketed drug in the future," and "the rapid increase in total opioid prescribing levels after the introduction of OxyContin in 1996 was driven by marketing and sales of opioids to physicians due to downplaying risks of harms associated with prescribing, including opioid use disorder and overdose." *Id.* at 10-11.

(10) the rates of adverse events associated with prescription opioids are greater than those associated with non-steroidal anti-inflammatory drugs (NASAIDs), *see id.* at 29-30.[9]

As part of her fifth opinion, *i.e.* that the increase in prescription opioid supply resulted in an exponential increase in prescription opioid overdose, Keyes makes statements regarding marketing causation. Specifically, in her five-page analysis of data showing "strong and statistically significant correlations" between opioid supply and opioid-related deaths, *id.* at 20-25, Keyes includes one paragraph which discusses pharmaceutical marketing. *See id.* at 22. In this paragraph, Keyes states that opioid pharmaceutical marketing was "often based on sources that underestimated the risk of opioid use disorder, harm, and diversion," which "contributed to the increase in the supply of opioids,"[10] and "led to consequences for opioid-related harm." *Id.*

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[9] Keyes also expresses opinions regarding abatement strategies. *See id.* at 30-40.

[10] To support her assertion that pharmaceutical marketing contributed to the increase in supply of opioids, Keyes cites to an article written by a medical doctor, which suggests that Purdue's aggressive marketing of OxyContin "likely" influenced doctors' prescribing practices. *See id.* at 22 (citing Van Zee A., "The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy," *Am. J. Public Health* (2009) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2622774/) (last checked August 22, 2019)). Keyes provides no analysis or information regarding whether this article was peer-reviewed, or the strength of the evidence contained therein. In the article, the author provides an "in-depth analysis of the promotion and marketing of OxyContin" and concludes that the drug's commercial success, which was fueled by an unprecedented promotion and marketing campaign, was stained by the OxyContin abuse and diversion that spread throughout the country. The author states Purdue spent an "unprecedented" amount of money promoting the drug, and physicians' interactions with pharmaceutical sales representatives have been found to influence prescribing practices. The author further states: "[a]lthough there are no available data for evaluating the promotional effect of free starter coupons for controlled drugs, *it seems likely* that the over- and misprescribing of a controlled drug are encouraged by such promotional programs and the public health would be well served by eliminating them." (emphasis added). The author concludes by suggesting that the FDA should review promotional and educational materials for truthfulness and accuracy before dissemination and that, at least in the area of controlled drugs, the pharmaceutical industry's direct role and influence in medical education should be severed.

Keyes further states: "[e]mpirical evidence has demonstrated that industry payments to physicians as part of the marketing of prescription opioids were *associated with* increased opioid prescriptions, and that 1 in 12 physicians in the US, and 1 in 5 family physicians, received opioid related marketing."[11] *Id.*

In her statements regarding marketing causation, Keyes discusses one study, published in 2019, which found that marketing in the form of payments to physicians "was associated with statistically significant increases in prescription opioid overdose." *Id.* (citing Hadland, Scott E., *et al.*, "Association of the Pharmaceutical Industry Marketing of Opioid Products With Mortality of Opioid-Related Overdoses," *JAMA Intern. Med.* (2019) ("Hadland (2019)") (https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2681059) (last checked August 22, 2019). Keyes states that the study: "demonstrated that even with statistical controls in place, each one standard deviation increase in payments to physicians was associated with statistically significant increases in prescription opioid overdose; including when marketing was assessed by marketing value in dollars per capita (each standard deviation increase associated with 1.09 times the rate of death), number of payments to physicians per capita (each standard deviation

[11] To support these assertions, Keyes cites four articles that were published in medical journals. *See* Keyes Rpt. at 22, 41 n.17, 44 n.69-71 (Doc. #: 1868-4). However, Keyes provides no analysis or information regarding whether the articles were peer-reviewed, or the strength of the evidence contained therein. *See id.* To support the assertion that opioid marketing payments to physicians were associated with increased opioid prescriptions, Keyes cites to one study, where the authors studied opioid marketing to physicians by examining their prescribing practices in the year following their receipt of industry marketing payments. *Id.* (citing Hadland, Scott E., *et al.*, "Association of the Pharmaceutical Industry Marketing of Opioid Products to Physicians with Subsequent Opioid Prescribing," *JAMA Intern. Med.* (2018) ("Hadland (2018)") (https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2681059 (last checked August 22, 2019)). There, the authors concluded that their findings established "*an association, not cause and effect,*" and noted that limitations in the study included the possibility of reverse causality, *i.e.* physicians who received industry payments may have been predisposed to prescribe opioids.

increase associated with 1.18 times the rate of death), and number of physicians receiving marketing per capita (each standard deviation increase associated with 1.12 times the rate of death)." *Id.* Keyes concludes: "[t]hese results are highly rigorous and clearly demonstrate harm to the population from opioid marketing and distribution." *Id.*

C. Analysis.

Defendants assert Keyes is not qualified to testify as an expert on marketing causation because she has no specialized expertise or experience in this field. *See* Defs. Mem. at 5 (Doc. #: 1862-2). Plaintiffs respond that Keyes is an expert in epidemiology, which "plays a role in describing the opioid epidemic and its causes." Pls. Opp. at 4 (Doc. #2166). Plaintiffs point out that Keyes "has extensive expertise on opioid-related harm, including large scale survey data and vital statistics analyses," and that she has published 19 peer-reviewed journal articles on opioid use and related harms.[12] *Id.*

[12] As an "example" of this work, Plaintiffs point to an article in which they contend Keyes "reported" that aggressive marketing contributed to the opioid epidemic. *See* Pls. Opp. at 4-5 (Doc. #2166); Pls. Ex. 3 (Doc. #: 2166-3) (M. Cerda, *et al.,* "Prescription Opioid Mortality Trends in NYC, 1990-2006," 132 *Drug Alcohol Dependency* (2013)). The focus of this article, however, was an epidemiological study of the changes in demographics and spatial patterns in overdose fatalities, induced by prescription opioids. *See* Pls. Ex. 3 at 1-10 (Doc. #: 2166-3). At the end of the article, the authors noted that early recognition of drug abuse patterns is critical to formulating strategies of prevention, and stated:

> Our findings suggest that in order to prevent the development of a prescription opioid epidemic, steps in the 1990s to increase the availability and use of analgesics, *including aggressive marketing* of potent formulations such as oxycodone hydrochloride and efforts to encourage clinicians to be more proactive in identifying and treating chronic pain, should have been accompanied by stricter measures to regulate sales of analgesics and to prevent the proliferation of illicit high-volume prescribers.

Id. at 10 (emphasis added). Although the article refers to "aggressive marketing," it contains no analysis or findings on this topic. *Id.*

As an epidemiologist, Keyes clearly has specialized training and expertise in statistical analysis and the determination of factors that play a role in producing opioid-related harm. The record, however, does not show that her expertise in the scientific field of epidemiology includes the determination of marketing factors that contributed to the increased supply in prescription opioids. *See* Keyes Rpt. at 7 (Doc. #: 1868-4) ("epidemiology" is the "science of understanding the causes and distributions of population health" that examines "the dynamic nature of populations and how health and diseases arises within them, as well as the conditions that shape population health over time and space, including policies, practices, and politics that create conditions that improve or deteriorate population health"). As discussed above, as a small portion of her larger opinion that the increase in opioid supply caused an increase in opioid-related deaths, *see* Keyes Rpt. at 720-25 (Doc. #: 1868-4), Keyes opines that pharmaceutical marketing contributed to the increased supply and, thus, led to opioid-related harm. *See id.* at 22. To support this conclusion, Keyes cites to one study that demonstrated a statistically significant connection between payments to physicians and increases in opioid-related overdoses. *See id.* at 22 (citing Hadland (2019)). Although Keyes states the results of this study "are highly rigorous and clearly demonstrate harm to the population from opioid marketing and distribution," *id.* at 22, her Report does not indicate that, in formulating this opinion, Keyes performed the methodology that is standard in the scientific process of her field of expertise, *i.e.* epidemiology. *See id.* at 8-10; *see also* Reference Manual on Scientific Evidence, Reference Guide on Epidemiology at 575 (Fed. Judicial Ctr. 3d ed. 2011) (any single study, even a clinical trial, is subject to the play of chance). In other words, Keyes has not shown that she applied epidemiological methods to determine that a cause-effect relationship may be inferred from the study that she cites. *See, e.g., Welding Fume Prods.*, 2005 WL 1868046, at 32 n.75 (the Bradford Hill factors "guide epidemiologists in making

judgments about whether a cause-effect relationship may be inferred from an association."); Ref. Manual at 598 ("epidemiology cannot prove causation; rather, causation is a judgment for epidemiologists and others interpreting the epidemiologic data").

On this record, plaintiffs have not shown that Keyes is qualified through "knowledge, skill, experience, training, or education" to offer opinions regarding pharmaceutical marketing causation. Fed. R. Evid. 702. While Keyes is clearly a distinguished expert in the field of epidemiology, *i.e.* the "science of understanding the causes and distributions of population health," plaintiffs have not shown that this expertise includes determining the effect of pharmaceutical marketing on doctors' prescribing practices, *see Rose,* 611 F. Supp.2d at 749 (expert's training and qualifications must relate to the subject matter of her proposed testimony), or that, in formulating her opinions on marketing causation, Keyes performed the methodology that is standard in the scientific field of epidemiology. *See, e.g., Kumho Tire Co. v. Carmichael,* 526 U.S. 137, 152 (1999) (expert must employ the same level of intellectual rigor that characterizes the practice of an expert in the relevant field). Accordingly, Keyes may not testify regarding the effect that Defendants' marketing efforts had on the sales and/or supply of prescription opioids.[13] This ruling applies narrowly, only to a small portion of Keyes' opinions – namely, the opinion contained in the first full paragraph on page 22 of her Report, in which she finds that Defendants' marketing efforts caused an increase in the supply of prescription opioids. *See* Keyes Rpt. at 22 (Doc. #: 1868-4). The Court's ruling does not in any way affect Keyes' remaining opinions.

[13] In light of this ruling, the Court does not address Defendants' arguments that Keyes' opinions on marketing causation are unreliable and unfairly prejudicial.

IV. Conclusion.

For the foregoing reasons, Defendants' Motion to Exclude the Marketing Causation Opinions of Mark Schumacher, Anna Lembke, and Katherine Keyes (**Doc. #: 1868**) is **GRANTED:** Schumacher, Lemke, and Keyes may not testify as experts regarding the narrow issue of marketing causation, *i.e.* the effect that Defendants' marketing efforts had on the sales and/or supply of opioids. This ruling does not impact the remainder of their opinions in any way.

IT IS SO ORDERED.

/s/ Dan Aaron Polster *August 27, 2019*
DAN AARON POLSTER
UNITED STATES DISTRICT JUDGE